

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following commentary.

I. Introduction

Claim 14 has been amended to set forth the claimed subject matter more clearly. The original specification supports these revisions, for example, in paragraphs [0047], [0050], [0052], [0318], [0365], and [0378] of the published application. Claims 16 and 22 are cancelled in view of the amendments to claim 14. Claims 1-13 were previously cancelled. Applicants reserve the right to file one or more continuation or divisional applications to pursue the subject matter of any cancelled claims. Claims 23 and 24 have been added, with ample support in the specification. See, for example, in Examples 2 and 7.

Applicants respectfully request entry of the amendment because no new matter has been introduced by way of this amendment. Upon entry, claims 14-15, 17-21, and 23-24 will be pending, with claims 19-21 withdrawn.

II. Rejection of Claims under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 14-18 and 22 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description (final Office action, sections 14-16) and for alleged lack of enablement (*Id.*, sections 25-26). Claims 16 and 22 are cancelled, thereby rendering the issue moot. Applicants respectfully traverse the rejection of the remaining claims.

The Examiner contends that the specification is enabling for making eukaryotic cells comprising certain altered cargo receptors but not any cargo receptors, and that a common structure or function for the genus of cargo receptor is lacking.

In the amended claim 14, a eukaryotic cell comprising heterologous DNA coding for the cargo receptor is characterized structurally, *i.e.* by an alteration of at least one amino acid in a

sequence of 9 amino acids of the carbohydrate recognition domain, exclusive of the two conserved amino acids. The claimed eukaryotic cell is also characterized functionally, *i.e.*, by its expression of a glycoprotein with a modified carbohydrate moiety comprising at least one glycoform selected from the group consisting of D-Gal, D-Man, D-Glc, D-GlcNAc, L-Fuc, SA, and D-GalNAc.

The specification is enabling for the amended claim 14 because it provides description on introducing random mutations into the specified carbohydrate recognition domain by constructing the random library and transfecting the eukaryotic cells as well as selecting and confirming the desired cells based on the carbohydrate moiety of the cargo receptor. See examples in the specification.

Accordingly, rejection of the claims under 35 U.S.C. § 112, first paragraph, should be withdrawn in view of the claim amendments.

III. Rejection of Claims under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 14-18 and 22 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Claims 16 and 22 are cancelled, thereby rendering the issue moot. Applicants respectfully traverse the rejection of the remaining claims.

Specifically, claim 14 is rejected because it is unclear to the Examiner to which entity the term “its” is referring. Applicants have amended claim 14 to recite clearly that the entity in question is the native cargo receptor.

The Examiner also contends that the definition for the term “cargo receptor” is unclear. Applicants have amended claim 14 to tie the “cargo receptor” with specific SEQ ID NOs.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

IV. Rejection of Claims under 35 U.S.C. § 102(b)

The Examiner rejected claims 14 and 16-18 under 35 U.S.C. § 102(b) for alleged anticipation by Ueno *et al.* (Nihon Yakugakkai Dai 121 nenkai Yoshishu, page 9, Abstract), and claims 14-18 and 22 for alleged anticipation by Hirai *et al.* (Nihon Yakugakkai Dai 121 nenkai Yoshishu, page 7, Abstract), respectively. Applicants respectfully traverse each rejection.

The claimed invention is informed by the discovery that carbohydrate moieties of a glycoprotein, which is on the surface of a eukaryotic cell and is secreted from the cell, are modified by alteration of the carbohydrate recognition domain of a cargo receptor. Thus, the alteration of a cargo receptor leads to changes in carbohydrate chains recognized by the cargo receptor and to changes in carbohydrate modification process. See paragraph [0047] of the published application. Specifically, the carbohydrate recognition domain of a cargo receptor is modified randomly to have a sequence of DXXXNXXXX, where X represents any amino acid residue. The eukaryotic cells, including animal cells such as MDCK cells and CHO cells, express DNA encoding the modified cargo receptor, which has different carbohydrate-binding specificity from its native counterpart. See Examples 4, 10 and 11. In contrast, the modified cargo receptor maintains its function of selectively transporting glycoproteins, as the native cargo receptor does.

The claimed invention is distinguished from the cited references in at least the following aspects:

A. The cited art does not teach the cargo receptor of the claimed invention.

Ueno discloses recombining the lectin domain of ERGIC-53 with MAH lectin or BPA lectin to generate various recombinants ERGIC-53 and then examining the localization of the recombinants by lectin staining. Similarly, Hirai describes that the lectin domain of VIP36 is recombined with MAH lectin or BPA lectin, and then the intracellular kinetics and localization of the recombinants are examined. Neither of these references teaches a eukaryotic cell

comprising heterologous DNA coding for a modified cargo receptor that is characterized by an alteration of at least one amino acid, relative to a native cargo receptor, wherein the alteration is in the sequence of the native cargo receptor's carbohydrate recognition domain, between amino acid residues 152 and 160 of SEQ ID NO: 2, exclusive of the conserved residues at positions 152 and 156, or between amino acid residues 162 and 170 of SEQ ID NO: 4, exclusive of the conserved residues at positions 162 and 166, as recited in claim 14.

For this reason alone, the claimed invention is not anticipated by the cited art because the prior art does not teach each and every aspect of the invention. The claimed invention is also patentable in view of the additional evidence detailed below.

B. In contrast to the modified cargo receptor of the invention, the recombinant proteins of the cited reference are not capable of selectively transporting glycoproteins.

The recombinant ERGIC-53 proteins of Ueno and the recombinant VIP36 proteins of Hirai are not capable of selectively transporting glycoproteins in eukaryotic cells. This is because the recombinants of Ueno and Hirai are localized in Golgi but cannot mobilize into the cell. As evidenced by the summary for the presentation of a Master's thesis by Yohko Takimori (University of Tokyo, Kashiwa campus, Chiba, Japan, February 16-18, 2004; Exhibit A), recombinant MAH/VIP36 and BPA/VIP36 proteins are localized in Golgi, and therefore, cannot transport glycoproteins. See last six lines at page 2. By the same token, the skilled artisan would not have expected that the similar recombinant ERGIC-53 proteins are capable of selectively transporting glycoproteins. By contrast, the modified cargo receptor of the invention is capable of selectively transporting the glycoprotein in said cell, as recited by claim 14.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of claims under 35 U.S.C. § 102 (b).

V. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

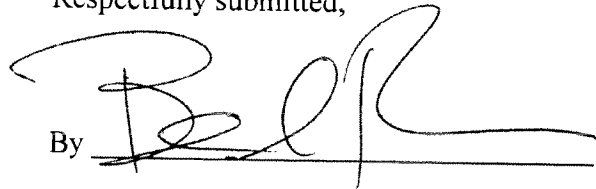
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Date June 27, 2007

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